REMARKS

Interview request

Applicants respectfully request a telephonic interview after the Examiner has reviewed the instant response and amendment. Applicants request the Examiner call Applicants' representatives David Devernoe at 858 720 7943 or Gregory Einhorn at (858) 720-5133.

Status of the Claims

Pending claims

Claims 21, 26 to 29, 31 to 35, 38-42, and 44-53 are pending and under consideration. Claim 51 has been withdrawn from consideration.

Allowed and objected to claims

Applicants thank the Examiner for finding that claims 21, 31-33 and 44-47 would be allowable if submitted in a separate, timely filed amendment, and only objecting to claim 29.

Claims amended and added in the instant amendment

Claims 54 to 56 have been added. Accordingly, after entry of the instant amendment, claims 21, 26 to 29, 32 to 35, 38 to 42, and 44 to 50 and 52 to 56 will be pending and under consideration.

Applicants respectfully request entry of the amendments set forth in this reply under 37 CFR §1.114. The amendment places the case in condition for allowance and does not raise any issues of new matter; and, the amended and new claims do not present new issues requiring further consideration or search.

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Outstanding Rejections

The rejection of claim 48 under 35 U.S.C. §112, second paragraph, is maintained. Claims 26-28, 34-35, 38-42, 48-50, 52 and 53 remain rejected under 35 U.S.C. §112, first paragraph. Claims 26-28, 48-49 and 52-53 are rejected under 35 U.S.C. §102.

Applicants respectfully traverse all outstanding rejections of the claims.

Support for the Claim Amendments

Support for the new and amended claims can be found throughout the application for the skilled artisan. For example, support for claims directed to oligonucleotide probes that hybridize under specific conditions can be found, inter alia, page 9, line 24, to page 10, line 6, of the specification. Support for claims directed to oligonucleotide probes of varying lengths can be found, inter alia, in the third paragraph of page 12. Applicants submit that no new matter is introduced by the instant amendment.

Issues under 35 U.S.C. §112, second paragraph

The rejection of claim 48 under 35 U.S.C. §112, second paragraph, for allegedly being indefinite, is maintained for reasons as set forth on page 3 of the non-final office action.

The term "stringent conditions"

The Patent Office alleges that claim 48 is indefinite in the recitation of "stringent conditions." In response, the Applicants direct the Office's attention to the specification at page 10, first full paragraph. Therein the Applicants' incorporate by reference J. Sambrook et al., Molecular Cloning, A Laboratory Manual (2d ed., 1989), which sets forth exemplary and well-known stringent hybridization conditions. Notably, this reference is incorporated merely to indicate the state of the art. *See, e.g.*, pages 11.45-11.57.

The instant amendment also addresses this issue.

In light of the foregoing amendments and remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 48 based upon 35 U.S.C. §112, second paragraph.

Issues under 35 U.S.C. §112, first paragraph

Written Description

Claims 26-28, 34-35, 38-42, 48-50, 52 and 53 remain rejected under the written description requirement of 35 U.S.C. §112, first paragraph.

The Patent Office remains concerned that because the functional limitation (esterase activity) is directed to the target nucleic acid to which the probe of the invention binds, the probe may also bind to a nucleic acid not encoding an esterase. The Patent Office notes that Applicants' amendment to the claims (of February 14, 2004) add functional limitations to the target nucleic acid to which the probe binds, rather than limiting the claimed probe to encoding an esterase-encoding sequence. The Patent Office alleges that the ability to bind to a particular sequence is not a function at all but merely defines the possible structure(s) of the compound. It is alleged that the presence of the ability to bind does not correlate to an ability to detect an esterase-encoding sequence because the presence of structural similarity to a sequence does not provide an assurance of functional identity (please see the instant Office action, pages 2-3). The Patent Office further alleges that the claimed oligonucleotides will bind to both esterase encoding sequences and non-esterase encoding sequences, and thus, any reliance on the similarity of the pending claims to Example 14 of the Written Description Guidelines (as an indication that adequate description is provided) is misplaced.

Applicants respectfully aver that one of ordinary skill in the art using the teaching of the specification would have been able to ascertain the scope of the claimed probes with reasonable clarity and would have recognized that Applicants' were in possession of the claimed invention at the time of filing. In addition to Example 14, Applicants respectfully aver that guidelines as set forth in Example 9 of the USPTO Written Description Guidelines indicate that the instant claimed

invention is adequately described. *See* 66 Fed. Reg. 1099 (2001) ("the Guidelines" or "Example 9", pages 35 to 37) (attached hereto as Exhibit A). Example 9 describes a situation involving a claim to a genus of nucleic acids that specifically hybridize (under highly stringent conditions) to the complement of a specifically described sequence (SEQ ID NO:1). In Example 9, SEQ ID NO:1 was disclosed in the specification as encoding a protein having a known function. In addition, an example was provided in the specification involving the use of the complement of SEQ ID NO:1 to isolate nucleic acids via hybridization. These isolated nucleic acids were not sequenced, however, they were expressed and "several" (i.e., not all) were shown to encode proteins having activity similar to SEQ ID NO:1. A single species was disclosed within the scope of the claimed genus comprising a molecule consisting of SEQ ID NO:1. The relevant art indicated that hybridization techniques using known DNA as a probe under highly stringent conditions were conventional in the art. The Guidelines indicate that adequate written description was provided.

Significantly, Example 9 is silent with regard to the number and percentage of sequences that did not encode proteins having activity similar to SEQ ID NO:1. Moreover, Example 9 is silent with regard to the percent identity the nucleic acids shared with SEQ ID NO:1. The Guidelines indicate that adequate written description was provided based on the use of hybridization language, the "encoding function" of DNA, and the level of skill in the art. The Guidelines indicate that importation of specific hybridization conditions (which describe the particulars of the high stringency hybridization) into the claim text is not required to meet the written description requirements. The Guidelines state that because a person of skill in the art would not expect substantial variation among species encompassed within the scope of the claims because the highly stringent conditions yield structurally similar DNAs, a representative number of species (one species in Example 9) is disclosed, and the claimed invention is adequately described.

Although not identical, the present claims are sufficiently analogous to Example 9 of the Guidelines to indicate that the instant claimed invention is adequately described in the specification. The structure of SEQ ID NO: 23 and the function of its encoded protein, SEQ ID NO:33, are described in the specification. The instant disclosure clearly contemplates the isolation (via hybridization) of nucleic acids that encode proteins having esterase activity using the claimed

probes, even if these nucleic acids are less than 100% identical to SEQ ID NO:23. Examples are provided to evaluate the activity of proteins encoded by the isolated nucleic acids. And, similar to Example 9 in the Guidelines, the level of skill in the art is high, and an artisan would understand hybridization techniques in accordance with the materials and limitations provided in the claims. The highly stringent conditions of Example 9 are sufficiently analogous to the stringent conditions of the instant claimed invention such that a person of skill in the art would not expect substantial variation among species encompassed within the scope of the instant claims because the claimed stringent conditions yield structurally similar DNAs. Accordingly, the facts and conclusion of Example 9 of the USPTO written description guidelines dictate that the instant claimed probes satisfy the written description requirement of section 112.

Applicants respectfully aver that the genus of probes of the instant invention is defined via shared physical and structural properties (stringent hybridization and exemplary sequences) in terms that "convey with reasonable clarity to those skilled in the art that Applicant, as of filing date sought, was in possession of invention." Vas-Cath Inc. V. Mahukar, 19 USPQ2d 1111, (Fed Cir. 1991).

Similarly, in this court's most recent pronouncement, it noted:

> More recently, in Enzo Biochem, we clarified that Eli Lilly did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure.

Amgen, 314 F.3d at 1332 [Amgen Inc. v. Hoechst Marion Roussel Inc., 314 F.3d 1313, 1330, 65 USPQ2d 1385, 1397 (Fed. Cir. 2003)]. (emphasis added)

Moba, B.V. v. Diamond Automation, Inc., 325 F.3d 1306, 1321, 66 USPQ2d 1429, 1438-9 (Fed. Cir. 2003).

Analogously, the functional limitation of the instantly claimed probes is sufficiently correlated to a particular, known structure (the exemplary sequence) and a physical (physico-

chemical) property (percent sequence identity or stringent hybridization). Accordingly, the probes of the instant invention are defined via shared physical and structural properties in terms that convey with reasonable clarity to those skilled in the art that Applicants, as of the filing date and at the time of the invention, were in possession of the claimed invention.

Accordingly, Applicants respectfully submit that the pending claims meet the written description requirement under 35 U.S.C. §112, first paragraph, and the rejection can be properly withdrawn.

Enablement

Claims 26-28, 34-35, 38-42, 48-50, 52 and 53 remain rejected under the enablement requirement of 35 U.S.C. §112, first paragraph.

The Patent Office notes that the specification enables a probe consisting of a fragment of SEQ ID NO:23 which will hybridize to SEQ ID NO:23 under stringent conditions and optionally a detectable label.

However, it is alleged that the specification does not enable a genus of probes that hybridizes to any nucleic acid having at least 90% sequence identity to SEQ ID NO:23 and encoding an esterase. The Patent Office remains concerned that because the claims allegedly recite low stringency hybridization conditions, it would take undue experimentation to use most of the claimed probes as asserted in the specification.

To address these concerns, the Applicants have amended the appropriate claims to add the limitation that the probes hybridize under "stringent conditions" (as expressly defined by the specification) to nucleic acids encoding a polypeptide having esterase activity. Accordingly, Applicants respectfully submit that after entry of the instant amendment the pending claims meet the enablement requirement of section 112, first paragraph.

Issues under 35 U.S.C. §102

The rejection of claims 26 to 43, 48 to 50, 52 and 53 under 35 U.S.C. §102 (a or b), as allegedly anticipated by Kim, et al., *J. Biol. Chem.* (1992) 267(11): 7710-7717 ("*Kim*"), or GenBank Accession No. X86487 ("*X86487*") has been maintained. The Patent Office invites further explanation as to why the claimed nucleic acids, at least 30 nucleotides in length, are not anticipated by the cited nucleic acid sequences, which allegedly contain only 18 or 23 consecutive residues similar to a nucleic acid of the claimed invention.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. Verdegaal Bros. v. Union Oil Co. of California, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

To address the Examiner's concerns, Applicants have previously amended the appropriate claims to add a length limitation to address this issue. The Applicants currently introduce hybridization conditions, where appropriate, which further distinguish the claims from the cited references.

The Office submits that since each of the nucleic acids of the cited references are each well over 30 nucleotides in length, the added/amended length limitation does not render the claims free of the cited references (please note the paragraph spanning pages 4 to 5 of the instant office action). *Kim* allegedly discloses a sequence that contains 18 nucleotides identical to bases 505-523 of SEQ ID NO:23. *X86487* allegedly discloses a sequence that contains 18 nucleotides identical to bases 360-378 of SEQ ID NO:23. Applicants have previously asserted that *Kim* fails to provide a teaching to select the particular 18 nucleotide sequence from more than the 5069 nucleotides in the entire cited sequence as a molecular probe. Similarly, the Applicants have previously asserted that *X86487* fails to provide a teaching to select the particular 18 nucleotide sequence from more than the 385 nucleotides in the entire cited sequence as a molecular probe.

Assuming, *arguendo*, that *Kim* and/or *X86487* teach the above nucleotide selection for use as a molecular probe; and also assuming, *arguendo*, that *Kim* and/or *X86487* teach 18- or 23-

residue long nucleotide sequences identical to particular portions of SEQ ID NO:23, the present claims are still not anticipated by either of these references. The hybridization and length limitations clearly differentiate the present claims from the cited sequences. For example, under stringent conditions, hybridization will occur only if there is at least 90% or 95% identity between the probe and the target sequences. *See* the specification at page 10, first full paragraph; page 13, first full paragraph. In a probe comprising at least 30 nucleotides, this means that identity must be present between at least 27 to 30 nucleotides of the probe and the target sequences. Notably, because the sequences allegedly having identity to SEQ ID NO:23 in *Kim* or *X86487* comprise only 18 or 23 nucleotides, identity between 27 to 30 nucleotides of *Kim* or *X86487* versus SEQ ID NO:23 is clearly not present. Thus, these sequences cannot anticipate the present claims. Accordingly, because neither *Kim* nor *X86487* are a single reference that teach each and every limitation of the claimed invention, the rejection under 35 U.S.C. §102 (a or b) can be properly withdrawn.

CONCLUSION

In view of the foregoing amendment and remarks, Applicants respectfully aver that the Examiner can properly withdraw the rejection of the pending claims under 35 U.S.C. §112, first and second paragraphs, and 35 U.S.C. §102. Applicants respectfully submit that all claims pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Applicants believe that no additional fees are necessitated by the present response and amendment. However, in the event any such fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 03-1952. Please credit any overpayment to this account.

As noted above, Applicants have requested a telephone conference with the undersigned representative to expedite prosecution of this application. After the Examiner has reviewed the instant response and amendment, please telephone the undersigned at 858 720 7943 or Gregory Einhorn at (858) 720-5133.

Dated: July 9, 2004

Respectfully submitted,

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e.g. expression vectors, the necessary common attribute is the ORF (SEQ ID NO: 2).

Weighing all factors including (1) that the full length ORF (SEQ ID NO: 2) is disclosed and (2) that any substantial variability within the genus arises due to addition of elements that are not part of the inventor's particular contribution, taken in view of the level of knowledge and skill in the art, one skilled in the art would recognize from the disclosure that the applicant was in possession of the genus of DNAs that comprise SEQ ID NO: 2.

Conclusion: The written description requirement is satisfied.

Example 9: Hybridization

Specification: The specification discloses a single cDNA (SEQ ID NO:1) which encodes a protein that binds to a dopamine receptor and stimulates adenylate cyclase activity. The specification includes an example wherein the complement of SEQ ID NO: 1 was used under highly stringent hybridization conditions (6XSSC and 65 degrees Celsius) for the isolation of nucleic acids that encode proteins that bind to dopamine receptor and stimulate adenylate cyclase activity. The hybridizing nucleic acids were not sequenced. They were expressed and several were shown to encode proteins that bind to a dopamine receptor and stimulate adenylate cyclase activity. These sequences may or may not be the same as SEQ ID NO: 1.

Claim:

An isolated nucleic acid that specifically hybridizes under highly stringent conditions to the complement of the sequence set forth in SEQ ID NO: 1,

wherein said nucleic acid encodes a protein that binds to a dopamine receptor and stimulates adenylate cyclase activity.

Analysis:

A review of the full content of the specification indicates that the essential feature of the claimed invention is the isolated nucleic acid that hybridizes to SEQ ID NO: 1 under highly stringent conditions and encodes a protein with a specific function. The art indicates that hybridization techniques using a known DNA as a probe under highly stringent conditions were conventional in the art at the time of filing.

The claim is drawn to a genus of nucleic acids all of which must hybridize with SEQ ID NO: 1 and must encode a protein with a specific activity.

The search of the prior art indicates that SEQ ID NO: 1 is novel and unobvious.

There is a single species disclosed (a molecule consisting of SEQ ID NO: 1) that is within the scope of the claimed genus.

There is actual reduction to practice of the disclosed species.

Now turning to the genus analysis, a person of skill in the art would not expect substantial variation among species encompassed within the scope of the claims because the highly stringent hybridization conditions set forth in the claim yield structurally similar DNAs. Thus, a representative number of species is disclosed, since highly stringent hybridization conditions in combination with the coding function of DNA and the level of

skill and knowledge in the art are adequate to determine that applicant was in possession of the claimed invention.

Conclusion: The claimed invention is adequately described.